Eszopiclone (Lunesta): a new nonbenzodiazepine hypnotic agent

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Randomized, placebo-controlled trials have shown that eszopiclone, a newly available nonbenzodiazepine hypnotic, effectively treats the symptoms of insomnia. Its pharmacokinetic and pharmacodynamic parameters are similar to those of the other currently available nonbenzodiazepine hypnotics (i.e., zolpidem and zaleplon). The unique quality of eszopiclone lies in its product labeling. It is not restricted to short-term use, unlike both zolpidem and zaleplon. Dosing of eszopiclone should begin at 2 mg for nonelderly patients and may be initiated at or increased to 3 mg if clinically indicated. The 3-mg nightly dose is more effective at sleep maintenance. Eszopiclone is well tolerated, with the main treatment-emergent side effects being unpleasant taste, headache, and dizziness. No studies comparing eszopiclone with nonpharmacologic insomnia treatments or other hypnotic agents, including zolpidem and zaleplon, are currently available.

The complaint of insomnia is defined as the perception of inadequate or nonrestorative sleep often related to difficulty initiating sleep, difficulty maintaining sleep, or frequent awakenings (1). It is typically classified as being either transient or chronic depending on the duration of a patient's symptoms. Transient insomnia, lasting only a few days, is often a result of acute stress, acute medical illness, jet lag, or self-medication (2). Insomnia lasting longer than 3 weeks is considered chronic and is usually multifactorial, resulting from chronic anxiety, depression, alcohol or substance abuse or withdrawal, medication use, or age-related changes in sleep. In hospitalized patients, additional factors contribute to poor sleep quality, including the anxiety associated with physical illness, nocturnal isolation from family members, and the disruptive effects of light, sounds, and procedures in the hospital.

Poor nocturnal sleep quality can have a deleterious impact upon patient comfort, mood, and ability to cooperate with hospital procedures. Therefore, ensuring adequate sleep quality within the hospital environment is a vital component of good patient care. Treatment of insomnia in hospitalized patients usually consists of both nonpharmacologic and pharmacologic approaches. Nonpharmacologic measures typically focus on treatment of the underlying factor(s) contributing to a patient's insomnia and may include, for example, establishing a regular schedule of sleeping and waking times (1). Pharmacologic treatment consists of the short-term use of hypnotic agents, such as benzodiazepines (e.g., temazepam, lorazepam, estazolam), benzodiazepine omega-1 receptor agonists (e.g., zolpidem and zaleplon), and trazodone (1). Other agents with sedative properties, such as antihistamines (e.g., diphenhydramine) and atypical antipsychotics (e.g., quetiapine), have also been used as pharmacological therapy for insomnia. The choice of agent should be based on pharmacokinetic and pharmacodynamic properties of the medication as well as patient-specific characteristics (1).

The Food and Drug Administration (FDA) approved oral eszopiclone on December 15, 2004. It is the S-isomer of zopiclone, which has been available in Europe since 1992 (3). Eszopiclone is the first of several new agents entering the US market for the treatment of insomnia. Other recently approved agents include the melatonin receptor agonist ramelteon (Rozerem) (4) and extended-release zolpidem (Ambien CR) (5). The purpose of this review is to examine the potential use of eszopiclone in managing insomnia in hospitalized patients.

INDICATION

Eszopiclone is indicated for the treatment of insomnia in patients ≥18 years of age. Unlike other nonbenzodiazepine agents, there is no restriction on its duration of use (6, 7).

PHARMACOLOGY

The precise mechanism of action of eszopiclone as a hypnotic is unknown, but its effect is believed to result from its interaction with GABA receptor complexes at binding domains located close to or allosterically coupled to benzodiazepine receptors. Eszopiclone is a nonbenzodiazepine hypnotic that is structurally unrelated to pyrazolopyrimidines, imidazopyridines, benzodiazepines, barbiturates, or other drugs with known hypnotic properties (6).

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PHARMACOKINETICS

Onset of action

In a study conducted by Zammit et al (8) in adults with chronic insomnia, the average onset of sleep (measured by sleep latency) was 10.4 minutes faster in the eszopiclone 2 mg group than in the placebo group.

Absorption and distribution

Eszopiclone is rapidly absorbed following oral administration. Peak plasma concentrations are achieved within 1 hour after oral administration. It is weakly bound to plasma proteins (52%–59%) (6).

Metabolism

Following oral administration, eszopiclone is extensively metabolized in the liver by oxidation and demethylation. The primary plasma metabolites have little to no binding potency to GABA receptors. In vitro studies have shown that CYP3A4 and CYP2E1 enzymes are involved in the metabolism of eszopiclone (6).

Elimination

The mean elimination half-life ($t_{1/2}$) of eszopiclone is approximately 6 hours. Less than 10% of an oral dose is excreted in the urine as parent drug (6).

Effect of food

In healthy adults, administration of a 3-mg dose of eszopiclone after a high-fat meal resulted in no change in area under the curve (AUC), a 21% reduction in peak concentration (C_{max}), and a 1-hour delayed time to reach peak concentration (t_{max}). The $t_{1/2}$ remained unchanged (6).

CLINICAL TRIALS

This section summarizes the three published clinical trials on the safety and efficacy of eszopiclone for the treatment of insomnia. All three trials enrolled patients who reported no more than 6.5 hours of sleep per night and who required more than 30 minutes to fall asleep each night for at least 1 month. Patients also met the criteria for primary insomnia given by the *Diagnostic and Statistical Manual of Mental Disorders—4th Edition, Text Revision* (DSM-IV):

A. The predominant complaint is difficulty initiating or maintaining sleep, or nonrestorative sleep, for at least 1 month.
B. The sleep disturbance (or associated daytime fatigue) causes clinically significant distress or impairment in social, occupational, or other important areas of functioning.
C. The sleep disturbance does not occur exclusively during the course of Narcolepsy, Breathing-Related Sleep Disorder, Circadian Rhythm Sleep Disorder, or a Parasomnia.
D. The disturbance does not occur exclusively during the course of another mental disorder (e.g., Major Depressive Disorder, Generalized Anxiety Disorder, a delirium).
E. The disturbance is not due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication) or a general medical condition (9).

Efficacy and safety of eszopiclone over 2 weeks in elderly patients

A randomized, double-blind, multicenter, placebo-controlled trial of eszopiclone was conducted in elderly patients, aged 65 to 85 years (10). A total of 231 patients were assigned to one of three treatment groups: placebo (n = 80), eszopiclone 1 mg (n = 72), or eszopiclone 2 mg (n = 79) nightly for 2 weeks. Patients reported results from a questionnaire each morning and evening through an interactive voice response system. Participants also returned to the clinic for weekly follow-up. The primary endpoint was sleep latency averaged over the double-blind period, and the primary analysis was the comparison between the eszopiclone 2 mg and placebo groups. Secondary endpoints included wake time after sleep onset, number of awakenings, sleep quality, sleep depth, total sleep time averaged over the double-blind period, and daytime function variables.

The eszopiclone 2 mg group had a significantly shorter sleep latency period compared with the placebo group over the double-blind period ($P = 0.0034$). The eszopiclone 2 mg group also had significantly longer total sleep time ($P = 0.0003$) compared with the placebo group. The eszopiclone 1 mg group had significantly shorter sleep latency ($P \leq 0.012$) compared with the placebo group, but there was no significant difference in total sleep time or any other secondary endpoint. Secondary analyses indicated that the eszopiclone 2 mg group had significantly less waking after sleep onset; significantly fewer and shorter daytime naps; and significantly higher ratings of sleep quality and depth, daytime alertness, and sense of physical well-being compared with the placebo group ($P < 0.05$). Based on these data, eszopiclone 1 mg was effective at inducing but not maintaining sleep, whereas the 2-mg dose was effective at both inducing and maintaining sleep.

Although both eszopiclone dose groups had shorter median sleep latencies at week 2 than at week 1, neither dose was significantly different from placebo at week 2 (eszopiclone 1 mg, $P = 0.10$; eszopiclone 2 mg, $P = 0.07$). This difference appeared to be due to improvement in the median sleep latency for the placebo group from week 1 to week 2 rather than a diminished effect for the eszopiclone 2 mg group. Eszopiclone 2 mg significantly increased patient-reported total sleep time compared with placebo at weeks 1 and 2 ($P \leq 0.002$). The eszopiclone 2 mg group had significantly higher quality ($P < 0.05$) and depth of sleep ($P < 0.05$) compared with the placebo group at weeks 1 and 2.

The most common (≥5%) treatment-related adverse event was unpleasant taste (eszopiclone 1 mg, 8.3%; eszopiclone 2 mg, 11.4%; placebo, 15.0%). Fewer subjects discontinued treatment because of adverse effects in the treatment groups than in the placebo group (eszopiclone 1 mg, 1.4%; eszopiclone 2 mg, 2.5%; placebo, 6.3%). There were no reported adverse events related to accidental falls, amnesia, or hallucinations.

Efficacy and safety of eszopiclone over 6 weeks

A randomized, double-blind, multicenter, placebo-controlled, parallel group trial conducted in adults aged 21 to 64 years assigned a total of 308 patients to one of three treatment groups:

placebo (n = 99), eszopiclone 2 mg (n = 104), or eszopiclone 3 mg (n = 105) nightly for 44 consecutive days (8). This was followed by 2 nights of placebo to assess the occurrence of rebound insomnia. Patients reported results nightly via an interactive voice response system and had overnight stays in the sleep laboratory for polysomnography recording. The primary endpoint was polysomnography-determined latency to persistent sleep. Secondary endpoints were mean sleep efficiency and wake time after sleep onset. Polysomnography data were reported as averages from nights 1, 15, and 29. Patient-reported sleep data were obtained from nights 1, 15, 29, and 43/44.

Both doses of eszopiclone significantly reduced the average latency to persistent sleep compared with placebo ($P < 0.001$). Secondary supportive analyses indicated that these treatment effects were consistent across nights 1, 15, and 29 ($P < 0.001$). Both doses of eszopiclone significantly improved the average sleep efficiency relative to placebo (3 mg, $P < 0.001$; 2 mg, $P < 0.01$). Additionally, 68% of patients in the eszopiclone 3 mg group ($P < 0.001$ vs placebo) and 53% of patients in the eszopiclone 2 mg group ($P < 0.03$ vs placebo) had polysomnography-defined total sleep time ≥7 hours (the double-blind average), compared with 37% of patients in the placebo group. These treatment effects were consistent across nights 1, 15, and 29 ($P < 0.01$) for the 3-mg dose.

Eszopiclone 3 mg, but not 2 mg, significantly reduced the double-blind average wake time after sleep onset relative to placebo ($P < 0.01$). Supportive analyses of eszopiclone 3 mg indicated that wake time after sleep onset was significantly less compared with placebo on nights 1 and 29, but not on night 15. The polysomnography-defined number of awakenings was not significantly different between treatment groups. Results of the double-blind average and nightly patient-reported sleep endpoints were consistent with the polysomnography findings. Eszopiclone 3 mg and 2 mg produced significantly less sleep latency ($P < 0.0001$ for both doses), higher quality of sleep ($P = 0.007$ and 0.04, respectively), and better depth of sleep ($P = 0.046$ and 0.005, respectively) relative to placebo. Eszopiclone 3 mg ($P = 0.02$ vs placebo), but not 2 mg, resulted in significantly less patient-reported wake time after sleep onset.

There was no evidence of tolerance or rebound insomnia after therapy discontinuation. Median digit symbol substitution test (DSST) scores showed no decrement in psychomotor performance relative to baseline and did not differ from placebo in either eszopiclone group.

The most common treatment-related adverse event was unpleasant taste, which was greatest in the eszopiclone 3 mg group. The rates of dizziness and somnolence in the eszopiclone 3 mg group were similar to those in the placebo group. No patient in the eszopiclone 3 mg group or the placebo group discontinued treatment due to adverse events; 3 patients in the 2 mg group discontinued for adverse events that may or may not have been related to the study drug. Rates of new adverse events occurring during the single-blind placebo run-out phase were lower in the eszopiclone groups (11.5% in the eszopiclone 2 mg group, 15.2% in the eszopiclone 3 mg group) than in the placebo group (18.2%). There were no differences between eszopiclone and placebo for central nervous system (CNS) and potentially CNS-related adverse events, the most commonly noted symptoms of hypnotic withdrawal.

Efficacy and safety of eszopiclone over 6 months

A randomized, double-blind, multicenter, placebo-controlled trial was conducted in patients aged 21 to 69 years and assigned a total of 788 patients to receive either eszopiclone 3 mg (n = 593) or placebo (n = 195) nightly for 6 months (11). Patients reported results weekly via an interactive voice response system. Monthly office visits were also scheduled for safety and compliance assessments. Endpoints included sleep latency; total sleep time; number of awakenings; wake time after sleep onset; quality of sleep; and next-day ratings of ability to function, daytime alertness, and sense of physical well-being. Seven time points (week 1 and months 1–6) during the study were analyzed. Data from week 1 were intended to measure short-term efficacy, while the remaining time points assessed sustained efficacy.

Compared with placebo, eszopiclone produced a statistically significant improvement ($P < 0.05$) in all of the aforementioned endpoints. These differences were evident at the first measured time point (week 1), as well as the subsequent 6 time points. At week 1, patients taking eszopiclone fell asleep a mean of 37.2 minutes faster, had 0.6 fewer nightly awakenings, experienced 0.9 fewer nights awake per week, and slept 50.2 minutes longer than patients in the placebo group. At 6 months, patients treated with eszopiclone fell asleep 16.1 minutes faster, had 0.7 fewer nightly awakenings, experienced 0.8 fewer nights awake per week, and slept 39 minutes longer.

Over the 6-month study period, adverse events were reported in 81.1% of patients in the eszopiclone group and 70.8% of patients in the placebo group. The most common events in both groups were unpleasant taste, headache, infection, pain, nausea, and pharyngitis. The vast majority of infections (~85%) were related to the common cold, and none resulted in discontinuation from the study. Headache was the only adverse event reported in more than 10% of the patients in both groups. Over the 6-month period, the rate of discontinuation due to adverse events was 12.8% in the eszopiclone group and 7.1% in the placebo group ($P < 0.05$). The most common reasons were somnolence (2.2% for eszopiclone, 1.5% for placebo), depression (2.0% and 0%), unpleasant taste (1.7% and 0.5%), headache (0% and 2%), asthenia (1.0% and 1.5%), and insomnia (0% and 1.5%).

Following discontinuation of the drug, the overall rates of "new" events (those not seen during the treatment period or a worsening of an event) were similar between the eszopiclone group and the placebo group (11.2% and 10.7%, respectively). There were no reports of seizures, hallucinations, or perceptual-disturbance events that are commonly reported as withdrawal symptoms following discontinuation of sedative-hypnotic medications; there was one report of anxiety in the eszopiclone group.

All of the patients over 64 years of age in the 6-month trial were part of the eszopiclone 3 mg treatment group. This dose is

Table 1. Incidence (%) of treatment-emergent adverse events in a 6-week placebo-controlled study in non-elderly adults with Lunesta*

Adverse event	Placebo (n = 99)	Lunesta 2 mg (n = 104)	Lunesta 3 mg (n = 105)
Body as a whole			
Headache	13	21	17
Viral infection	1	3	3
Digestive system			
Dry mouth	3	5	7
Dyspepsia	4	4	5
Nausea	4	5	4
Vomiting	1	3	0
Nervous system			
Anxiety	0	3	1
Confusion	0	0	3
Depression	0	4	1
Dizziness	4	5	7
Hallucinations	0	1	3
Libido decreased	0	0	3
Nervousness	3	5	0
Somnolence	3	10	8
Respiratory system			
Infection	3	5	10
Skin and appendages			
Rash	1	3	4
Special senses			
Unpleasant taste	3	17	34
Urogenital system			
Dysmenorrhea†	0	3	0
Gynecomastia‡	0	3	0

*Reprinted with permission from reference 6. Events for which the Lunesta incidence was equal to or less than placebo are not listed on the table but included the following: abnormal dreams, accidental injury, back pain, diarrhea, flu syndrome, myalgia, pain, pharyngitis, and rhinitis.

†Gender-specific adverse event in females.

‡Gender-specific adverse event in males.

higher than the recommended dose (either 1 or 2 mg, depending on clinical factors) in the prescribing information.

None of the three trials studying the safety and efficacy of eszopiclone reported a power calculation. Therefore, it is unclear as to whether enough patients were included in each trial to truly show a difference between the treatment and placebo groups. Trials of the nature discussed here typically have a very high attrition rate; therefore, intention-to-treat analyses are most appropriate for this circumstance. Each of the three trials included an intention-to-treat population consisting of patients who received at least 1 dose of study medication.

Each study was sponsored and funded by Sepracor Inc., the manufacturer of eszopiclone. Several of the investigators were employees, speakers, or grant recipients of Sepracor Inc.; nonetheless, potential conflicts of interest were clearly disclosed in each study.

Table 2. Incidence (%) of treatment-emergent adverse events in elderly adults (ages 65–86) in 2-week placebo-controlled trials with Lunesta*

Adverse event	Placebo (n = 208)	Lunesta 1 mg (n = 72)	Lunesta 2 mg (n = 215)
Body as a whole			
Accidental injury	1	0	3
Headache	14	15	13
Pain	2	4	5
Digestive system			
Diarrhea	2	4	2
Dry mouth	2	3	7
Dyspepsia	2	6	2
Nervous system			
Abnormal dreams	0	3	1
Dizziness	2	1	6
Nervousness	1	0	2
Neuralgia	0	3	0
Skin and appendages			
Pruritus	1	4	1
Special senses			
Unpleasant taste	0	8	12
Urogenital system			
Urinary tract infection	0	3	0

*Reprinted with permission from reference 6. Events for which the Lunesta incidence was equal to or less than placebo are not listed on the table but included the following: abdominal pain, asthenia, nausea, rash, and somnolence.

ADVERSE EFFECTS

Table 1 summarizes the most common adverse events reported from a phase 3 placebo-controlled study in nonelderly patients treated with either eszopiclone 2 mg or 3 mg. Treatment duration in this trial was 44 days (6).

Table 2 shows the incidence of adverse events reported from combined phase 3 placebo-controlled studies with either eszopiclone 1 mg or 2 mg in elderly patients (aged 65 to 86 years). Treatment duration in these trials was 14 days (6).

The two most frequent adverse events in both treatment durations were headache and unpleasant taste. Dyspepsia, pain, and diarrhea were also common in elderly patients treated for 14 days, whereas somnolence, dry mouth, and nausea were common in adults treated for 44 days.

WARNINGS/PRECAUTIONS

While there are no known contraindications to eszopiclone (6), the drug should be administered with caution in patients exhibiting signs and symptoms of depression. Suicidal tendencies may be present, and intentional overdose is more common in such patients. Therefore, the smallest dose feasible should be prescribed to the patient. In clinical trials with eszopiclone, one case of overdose with up to 36 mg was reported in which the subject fully recovered.

In healthy volunteers, a 7-mg oral dose of eszopiclone did not produce respiratory-depressant effects. However, caution

should be exercised in administration of eszopiclone to patients with compromised respiratory function.

Use of benzodiazepines and similar agents may lead to physical and psychological dependence. The risk of abuse and dependence increases with the dose and duration of treatment and concomitant use of other psychoactive drugs. The risk is also greater in patients with a history of alcohol or drug abuse or history of psychiatric disorders.

Tolerance may develop after repeated use of benzodiazepines and benzodiazepine-like agents for a few weeks. However, no evidence of developed tolerance was seen with eszopiclone over a period of 6 months in clinical trials (6).

DOSING AND ADMINISTRATION

The recommended starting dose for eszopiclone for most nonelderly adults is 2 mg immediately before bedtime. Dosing can be initiated at or raised to 3 mg if clinically indicated, since 3 mg is more effective for sleep maintenance.

Taking eszopiclone with or immediately after a heavy, high-fat meal results in slower absorption and would be expected to reduce the effect of eszopiclone on sleep latency.

Dosing in special populations

The elderly: The recommended starting dose for elderly patients whose primary complaint is difficulty falling asleep is 1 mg immediately before bedtime. The dose may be increased to 2 mg if clinically indicated. For elderly patients whose primary complaint is difficulty staying asleep, the recommended dose is 2 mg immediately before bedtime.

Hepatic impairment: The starting dose should be 1 mg in patients with severe hepatic impairment. Eszopiclone should be used with caution in these patients.

Renal impairment: No dose adjustments are necessary in patients with any degree of renal insufficiency.

Coadministration with CYP3A4 inhibitors: The starting dose should not exceed 1 mg in patients coadministered eszopiclone with potent CYP3A4 inhibitors (see drug interactions section). If needed, the dose can be raised to 2 mg (6).

Pregnancy/lactation

Pregnancy category C: There are no adequate, well-controlled studies of eszopiclone in pregnant women. Eszopiclone should be used during pregnancy only if the potential benefits outweigh the potential risks.

It is not known whether eszopiclone is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when eszopiclone is administered to a nursing mother (6).

DRUG INTERACTIONS

CNS-active drugs

Ethanol: An additive impairment of psychomotor performance was seen with coadministration of eszopiclone and ethanol.

Paroxetine: Coadministration of single doses of eszopiclone 3 mg and paroxetine 20 mg daily for 7 days produced no pharmacokinetic or pharmacodynamic interaction.

Lorazepam: Coadministration of single doses of eszopiclone 3 mg and lorazepam 2 mg did not have clinically relevant effects on the pharmacokinetics or pharmacodynamics of either drug.

Olanzapine: Coadministration of single doses of eszopiclone 3 mg and olanzapine 10 mg produced a decrease in DSST scores, resulting from a pharmacodynamic interaction. The pharmacokinetics of both drugs were unaltered. No specific recommendation for dose adjustments of either drug is made by the manufacturer in the prescribing information.

Drugs that inhibit CYP3A4

The AUC of eszopiclone was increased 2- to 3-fold by coadministration of ketoconazole, a potent inhibitor of CYP3A4, 400 mg daily for 5 days. C_{max} and t_{max} were increased 1.4-fold and 1.3-fold, respectively. Other strong inhibitors of CYP3A4 (e.g., itraconazole, clarithromycin, nefazodone, ritonavir, nelfinavir) would be expected to behave similarly. However, no specific recommendations for dose adjustments are made in the prescribing information.

Drugs that induce CYP3A4

Racemic zopiclone exposure was reduced by 80% by concomitant use of rifampicin, a potent inducer of CYP3A4. A similar effect would be expected with eszopiclone. Nonetheless, the manufacturer provides no recommendations for dose adjustments when the two drugs are coadministered.

Drugs highly bound to plasma proteins

Eszopiclone is not highly bound to plasma proteins; therefore, the disposition of eszopiclone is not expected to be sensitive to alterations in protein binding. Administration of eszopiclone 3 mg to a patient taking another drug that is highly protein bound would not be expected to alter the free concentration of either drug.

Drugs with a narrow therapeutic index

Digoxin: A single dose of eszopiclone 3 mg did not affect the pharmacokinetics of digoxin measured at steady state.

Warfarin: Eszopiclone 3 mg administered daily for 5 days did not affect the pharmacokinetics of warfarin, nor were there any changes in prothrombin time following a single 25-mg oral dose of warfarin (6).

DOSAGE FORMS

Eszopiclone is available as 1-mg, 2-mg, and 3-mg tablets. It is a schedule IV controlled substance under the Controlled Substances Act (6).

PHARMACOECONOMICS

As shown in *Table 3,* the Baylor University Medical Center acquisition cost for eszopiclone ($2.88 per tablet, regardless of the strength) is slightly higher than, but comparable to, the costs of both zolpidem and zaleplon and is much higher than the costs of older hypnotic agents.

Table 3. Pharmacy acquisition costs of eszopiclone and other commonly used agents for the treatment of insomnia in hospitalized patients at Baylor University Medical Center

Drug name	Controlled substance category	Dosage (mg)	Unit cost ($)
Eszopiclone (Lunesta)*	IV	1	2.88
		2	2.88
		3	2.88
Zolpidem (Ambien)*,†	IV	5	2.51
		10	2.83
Zaleplon (Sonata)*,†	IV	5	2.07
		10	2.67
Temazepam (Restoril)*,†	IV	15	0.09
		30	0.13
Trazodone (Desyrel)†	N/A‡	50	0.04
		100	0.07
		150	0.10
Diphenhydramine (Benadryl)*,†	N/A‡	50	0.04
Quetiapine (Seroquel)†	N/A‡	25	1.53

*Approved by the Food and Drug Administration for the treatment of insomnia.
†Formulary agent.
‡Legend (i.e., prescription) medication but not a controlled substance.

CONCLUSIONS

The current data suggest that the use of eszopiclone in hospitalized patients offers no distinct advantage over other currently available hypnotics. Like other nonbenzodiazepine agents, eszopiclone has been shown to be efficacious in sleep induction and maintenance, and its pharmacokinetic and pharmacodynamic parameters are similar to those of zolpidem and zaleplon. Dosing should begin at 2 mg for nonelderly patients and may be initiated at or increased to 3 mg if clinically appropriate. However, there are currently no efficacy studies that directly compare eszopiclone with other hypnotic agents, including zolpidem or zaleplon, or with nonpharmacologic treatments. The acquisition cost of eszopiclone is comparable to the cost of zolpidem and zaleplon but much higher than that of older hypnotic agents. Lastly, the distinguishing feature of eszopiclone—approved labeling for long-term use—is not an overriding consideration in the decision to administer this medication to hospitalized patients.

1. Lenhart SE, Buysse DJ. Treatment of insomnia in hospitalized patients. *Ann Pharmacother* 2001;35(11):1449–1457.
2. Kupfer DJ, Reynolds CF III. Current concepts: management of insomnia. *N Engl J Med* 1997;336(5):341–346.
3. Eszopiclone: esopiclone, estorra, S-zopiclone, zopiclone—Sepracor. *Drugs R D* 2005;6(2):111–115.
4. Takeda Pharmaceuticals America, Inc. Rozerem™ prescribing information. Lincolnshire, IL: Takeda Pharmaceuticals America, Inc, 2005 August.
5. Sanofi-Synthelabo Inc. Ambien CR™ prescribing information. New York: Sanofi-Synthelabo Inc, 2005 September.
6. Sepracor Inc. Lunesta™ prescribing information. Marlborough, MA: Sepracor Inc, 2005 March.
7. Eszopiclone (Lunesta), a new hypnotic. *Med Lett Drugs Ther* 2005;47(1203): 17–19.
8. Zammit GK, McNabb LJ, Caron J, Amato DA, Roth T. Efficacy and safety of eszopiclone across 6-weeks of treatment for primary insomnia. *Curr Med Res Opin* 2004;20(12):1979–1991.
9. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders—Fourth Edition, Text Revision*. Washington, DC: American Psychiatric Association, 2000.
10. Scharf M, Erman M, Rosenberg R, Seiden D, McCall WV, Amato D, Wessel TC. A 2-week efficacy and safety study of eszopiclone in elderly patients with primary insomnia. *Sleep* 2005;28(6):720–727.
11. Krystal AD, Walsh JK, Laska E, Caron J, Amato DA, Wessel TC, Roth T. Sustained efficacy of eszopiclone over 6 months of nightly treatment: results of a randomized, double-blind, placebo-controlled study in adults with chronic insomnia. *Sleep* 2003;26(7):793–799.